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Original Research Article

Study on Outcome of Pregnancy in Patients with Unilaterally Increased Uterine Artery Resistance in Second Trimester

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Abstract:

Adverse pregnancy outcome due to impaired placentation have been shown to demonstrate increased impedance in the spiral artery. The spiral arteries are firstly invaded by trophoblasts and which then becomes incorporated into the vessel wall and replaces the endothelium and muscular layer. This results in the conversion of the small spiral arteries into vessels of greater diameter with low resistance and high compliance, in absence of maternal vasomotor control. This study was a Prospective Observational study, carried out in the Department of Obstetrics and Gynaecology, in JLNMCH, Bhagalpur, Bihar. The study population consisted of pregnant women between 18 – 20 weeks of gestation with viable pregnancy. During pregnancy, 63(18.36%) women developed hypertensive disorders. Among these 63 patients, 37(58.73%) women had increased uterine artery pulsatility index in second trimester scan and 26(41.26%) had normal pulsatility index. The results were comparable for gestational hypertension with normal and unilaterally increased uterine artery PI and were not statistically significant.

Keywords: Uterine Artery Resistance, Uterine Artery Pulsatility Index, Outcome.

Introduction

Doppler flow studies of the uterine artery provides an accurate means of assessing uteroplacental resistance to blood flow and a good method of assessing impairment or absence of uteroplacental blood flow. It is a useful modality to obtain vital information which is important to the clinician and the pregnant women for a subsequent approach.
Adverse pregnancy outcome due to impaired placentation have been shown to demonstrate increased impedance in the spiral artery.

The spiral arteries are firstly invaded by trophoblasts and which then becomes incorporated into the vessel wall and replaces the endothelium and muscular layer. This results in the conversion of the small spiral arteries into vessels of greater diameter with low resistance and high compliance, in absence of maternal vasomotor control. This vascular transformation in the uterus is necessary to ensure a dramatic increase in blood supply to the intervillous space. The impairment of this physiological process is associated with increased vascular resistance and increased impedance to blood flow and ultimately affect blood flow into the placenta. These sequences of events precede the onset of the complications. This process commences in the first trimester and ends in early second trimester. Uterine artery Doppler velocimetry alone or in combination with other biochemical markers can be used as a screening method for these disorders in second trimester. Because of the heterogeneity of the etiology of adverse pregnancy outcome like pre-eclampsia, fetal growth restriction, preterm labour and stillbirth, due to impaired implantation of placenta, there is no uniformity in favour of using uterine artery Doppler. The role of various uterine artery Doppler impedance indices to predict the pregnancy outcome in the second trimester had been evaluated over past few years, as a screening tool. However, these indices have been mainly analyzed as mean of the right and left side values, without taking into account the discordancy of the blood flow between the two sides.

The location of the trophoblastic reaction may also cause the difference between the two uterine arteries impedance indices, in which one artery develops the physiologic changes before the contralateral artery. Discordancy in the flow may result from an abnormally high resistance in one vessel resulting in adverse outcomes.It is well

known that in the first trimester and early second trimester, there is a considerable overlap between outcome of normal pregnancy and pregnancies that later develop preeclampsia, with the presence both notching and high pulsatility index values. The performance of uterine artery Doppler alone as screening marker increases gradually in the second trimester. Although screening at 23–24 weeks may detect most of the women who developed adverse outcome in the latter half of the pregnancy with the abnormal Doppler indices, it may fail in predicting certain women with adverse outcome. This is due to the fact that as abnormal Doppler at 20 weeks may become normal as the gestation advances, due to reduction in the resistance to the vascular flow, which was a physiological process. Another drawback of performing the uterine Doppler at 24 weeks is that this gestation is too late for intervention, to reduce the risk of the most severe cases of preeclampsia.

Studies on uterine artery Doppler, if performed in the early second trimester i.e. at the commencement of secondary wave of trophoblastic invasion, may help in screening and predicting early onset disorders resulting from utero-placental insufficiency. The objective of this study is to predict the outcome of pregnancy in women with unilaterally increased uterine artery resistance, in second trimester and evaluation of complications according to placental location.

Material and Methods

This study was a Prospective Observational study, carried out in the Department of Obstetrics and Gynaecology, Jawaharlal Nehru Medical College and Hospital, Bhagalpur, Bihar.

The study population consisted of pregnant women between 18 – 20 weeks of gestation with viable pregnancy.

Inclusion criteria

- Antenatal cases between 18-20 weeks of gestation with viable pregnancy
- Singleton pregnancy

Exclusion criteria

- Multiple pregnancy
- Anomalous fetus

Using probability of Type 1 error (α) as 0.05(5%) and power of test (1-β) as 0.9 (90%), with an expected overall incidence of obstetric complications of 15 percent among those with abnormal Doppler i.e. with unilateral increase in PI value of >1.5 and the mean PI <1.5 and 5 percent in those with normal Doppler. To reject the null hypothesis that pregnancy outcome will be the same among women with normal and abnormal Doppler, minimum of 200 women need to be studied. Antenatal patients between 18- 20 weeks of gestation who consented for undergoing uterine artery Doppler, and were willing for follow up, were recruited for the study. Written informed consent for doing this study was taken from all patients along with the consent for anomaly scan.

Data regarding the demographic profile of the patients, their past obstetric history and history of present pregnancy was collected. Routine antenatal check-up with general, systemic and obstetric examination of the patient was done. Routine target scan at 18-20 weeks was performed for the patients. Placental location was documented. Placenta was classified as central (if it crosses the maternal spine) and lateral (if present on either side of maternal spine).

Results

A total of 374 women were enrolled in the study. We lost follow up in eleven patients, and in twelve cases there was bilateral rise in pulsatility Index. Their outcome was also in favour of various studies done in the past, where they established that mean PI acts as a good screening tool in the prediction of adverse pregnancy outcome in high risk women. A prospective study done by Sergio et al, between 6-12 weeks, concluded that in patients with discordant uterine artery velocity waveforms, trophoblastic invasion is impaired, resulting in defective placentation and spontaneous miscarriages.

Currently, considering the same result we wanted to know, whether second trimester unilateral increase in PI of the uterine artery Doppler with normal mean PI, can have better sensitivity in predicting pregnancy outcome. Hence total of 343 cases that had unilateral increase in the pulsatility of uterine artery Doppler were followed and analyzed with the aforementioned maternal, fetal and neonatal outcome. Adverse pregnancy outcome included maternal, fetal or neonatal outcome. Adverse maternal outcome included in our study were Gestational hypertension, preeclampsia, eclampsia and abruption. Adverse fetal outcome included intrauterine growth restriction and still births, while adverse neonatal outcome included preterm deliveries, small for gestation age babies or NICU admissions due to preterm deliveries, low Apgar, with evidence of acidosis on arterial blood gas analysis or with neonates developing acute respiratory distress syndrome.

Table 1: Fetal/Neonatal and Maternal outcomes

Fetal Outcome	Neonatal	N(%)	Maternal Outcome	N(%)
Still Births		1(0.2)	Gestational Hypertension	47(13.90)
Live Births		342(99.70)	Preeclampsia	16(4.66)
IUGR		69(20.11)		
Preterm Delivery		34(9.94)	Abruption	1(0.81)
NICU Admissions		28(8.16)	Normal Outcome	280(81.63)
Normal Outcome		211(61.69)		

Taking into consideration all maternal and fetal outcomes, 138 (40.35%) out of 342 patients had one or more adverse outcome, while 205(59.76%) patients had a normal maternal and fetal outcome in pregnancy.

Table 2: Cases distribution based on unilateral increase in uterine

Artery Doppler (PI) in second Trimester			
Pregnancy Outcome	**Uterine A. Doppler Abnormal (PI>1.5)**	**Uterine A. Doppler Normal (PI<1.5)**	**P value**
n(%)	**n(%)**	**n(%)**	
343(100)	122(35.56)	221(64.43)	
Adverse Outcome			
138(40.23)	97(79.50)	41(18.55)	
Normal Outcome			0.000
205(59.76)	25(20.49)	180(81.44)	

***Chi Square test (Significant p value < 0.05**

Whenever there was raised unilateral uterine artery Doppler PI, the adverse pregnancy outcomes were increased by fourfold. Conversely, the percentage of patients with normal Doppler resulting in normal pregnancy outcome was also fourfold higher. There was statistical significant association between uterine artery Doppler and pregnancy outcome with $p<0.01$. These results establish the fact that most of the women with normal Doppler will have normal pregnancy outcome.

Table 3: Fetal outcome with uterine artery Doppler

Fetal Outcome	n=343	Uterine A. PI>1.5	Uterine A. PI<1.5
		n (%)	**n (%)**
		122(35.56)	221(64.43)
Still Births	1	0(0)	1(0.29)
Live Births	342	122(100)	220(99.54)

Among 122 patients with abnormal uterine artery Doppler, all had live births and no still births noted.

Conversely, one still birth was observed even with normal uterine artery Doppler. That patient was a case of dermatomyositis, who was diagnosed at 9 weeks of gestation and was started on prednisolone. This patient developed early onset intrauterine growth restriction. The umbilical artery Doppler was normal throughout. She had a sudden intrauterine death at 32 weeks. The cause of death was probably secondary to early onset IUGR.

The other causes of early onset of IUGR like aneuploidies could have contributed to the intrauterine death.

Table 4:Uterine artery Doppler (PI) - Pregnancy Outcome

Outcome variable	Uterine A Doppler Abnormal (PI>1.5)	Uterine A Doppler Normal (PI>1.5)	P value
	n(%)	**n(%)**	
n=343	122(35.56)	221(64.43)	0.604
Gestational	22(18.03)	25(11.31)	
Hypertension (47)			
Preeclampsia (16)	15(12.29)	1(0.45)	0.000
Abruption (1)	1(0.81)	0(0)	0.177
IUGR (<10th centile) (69)	48(39.34)	21(9.5)	0.000

***Chi Square test (Significant p value < 0.05)**

During pregnancy, 63(18.36%) women developed hypertensive disorders. Among these 63 patients, 37(58.73%) women had increased uterine artery pulsatility index in second trimester scan and

26(41.26%) had normal pulsatility index. The results were comparable for gestational hypertension with normal and unilaterally increased uterine artery PI and were not statistically significant. Fifteen (93.75%) cases with unilateral raised PI developed preeclampsia which indicates a strong association of preeclampsia with unilaterally increased uterine artery PI, which was statistically significant (p<0.005).Ten (15.87%) out of these 63 patients had early onset preeclampsia, six (9.5%) had late onset preeclampsia, while the rest 47 (74.60%) had Gestational HTN. 15(23.80%) women had increased uterine artery pulsatility index in second trimester scan (P<0.01), while one patient had normal pulsatility index. One woman who had normal Pulsatility index developed late onset preeclampsia at 36+ weeks. Twenty three women developed gestational hypertension ≥ 36+ weeks. These could be due to the atherosclerotic changes in the placental vasculature that occur at term, resulting in failure of placenta function. Hence the uterine artery PI might be normal in those women. There was no case of eclampsia. One woman had abruption.

This patient who developed abruption at 32 weeks had early onset preeclampsia for which an Emergency LSCS was done. She was elderly (41year old), obese, had overt diabetes, developed early onset preeclampsia. All these risk factors could have caused abruption. Neonate was admitted in NICU and was intubated in view of prematurity and acidosis on arterial blood gas analysis. Baby received surfactant and was extubated on day 4 and was discharged in a stable condition on day 35 of life.

The above results were indicating strong association with abnormal Doppler which was statistically significant (p<0.001). These results suggest that uterine artery Doppler had good negative predictive value in ruling out adverse maternal outcome.

Discussion

In our study, we recruited 374 women and after exclusions, 343 women were followed throughout the pregnancy. Both maternal and the perinatal outcome were evaluated. Our study was done between 18-20 weeks. We found the mean Pulsatility index of right-left uterine artery as 1.74± 0.26 in study group and 0.88 ± 0.22 in control group.

E. Contro et al conducted a case-control study in 262 viable pregnancies between 20 and 22 weeks of gestation. They obtained the mean Pulsatility index of right–left uterine artery and was 1.12 ± 0.25 in study group and 0.92 ± 0.24 in control group.

We found 122 women with abnormal uterine artery Doppler i.e. with unilaterally raised Pulsatility Index (>1.5) and with mean Pulsatility index of <1.5.

Abnormal outcome included ninety seven women (87.70%) out of 122 cases with abnormal Doppler. Twenty five (12.29%) women with abnormal Doppler had normal outcome. Statistically significant association was observed between abnormal Doppler and adverse pregnancy outcome (P<0.01).In the study done by E. Contro et al, preeclampsia occurred in 7/262 (2.6%) women, Caesarean section due to fetal distress was performed in 15/262 (5.7%) women. There was equal distribution of cases in both the study and control group with respect to preeclampsia and low birth weight and the results were not significantly different. They concluded that, if the mean Pulsatility Index is normal then obstetric and perinatal outcome expected to be uneventful.

In our study, Preeclampsia occurred in 16/343(4.66) women, out of whom fifteen had abnormal Doppler and one with normal Doppler. In contrast to E Contro et al we found a statistically significant relationship between abnormal Doppler and occurrence of preeclampsia, 15/343(4.37) with p value <0.05.

During pregnancy, 63(18.36%) women developed hypertensive disorders. Among these 63 patients, 37(58.73%) women had increased uterine artery pulsatility index in second trimester scan and 26(41.26%) had normal pulsatility index. The results were comparable for gestational hypertension with normal and abnormal Doppler and were not statistically significant.15(93.75%) cases with unilateral raised PI developed preeclampsia which indicates a strong association of preeclampsia with abnormal Doppler which was statistically significant (p<0.005).

Ten (15.87%) out of these 63 patients had early onset preeclampsia, 6(9.5%) had late onset preeclampsia, while the rest 47 (74.60%) had Gestational HTN. 15(23.80%) women had increased uterine artery pulsatility index in second trimester scan (P<0.01) while one patient had normal pulsatility index. One women who had normal Pulsatility index developed late onset preeclampsia at 36+ weeks. Twenty three women developed gestational hypertension at and after 36+ weeks. These could be the atherosclerotic changes in the placental vasculature resulting in failure of placenta function. Hence the uterine artery PI might be normal in those women. There was no case of eclampsia. One woman had abruption.

This patient who developed abruption at 32 weeks had early onset preeclampsia for which an emergency LSCS was done. She was elderly (41year old), obese, had overt diabetes, developed early onset preeclampsia. All these risk factors could have caused abruption. Neonate was

admitted in NICU and was intubated in view of prematurity and acidosis on arterial blood gas analysis. Baby received surfactant and was extubated on day 4 and was discharged in a stable condition on day 35 of life.

The above results obtained in relation to preeclampsia were consistent with the results obtained by the study done by Aardema et al. Various studies done in the past by Bower et al, Harrington et al, who used various indices of uterine artery Doppler, to predict the pregnancy outcome of preeclampsia were not able to prove the association between them. In contrast to their studies, we were able to establish a significant relationship between preeclampsia and abnormal Pulsatility index in consistent with those by Aardema et al.

In our study, in one hundred and twenty two abnormal Doppler cases, 39 women (31.96%) underwent caesarean section due to fetal distress, Preterm delivery (<37 weeks) in 28(22.95%) cases and small for gestation (< 10^{th} centile) in 48(39.34%) cases. Preeclampsia was observed in 15 cases (12.29%).

In our study, sixty nine (20.11%) babies were growth restricted, of which three had symmetrical IUGR and remaining sixty six had asymmetrical IUGR. Thirty six patients (10.49%) developed oligohydramnios during the pregnancy, of which fifteen patients had coexisting fetal growth restriction. Ten of them had coexisting preeclampsia and eight with gestational hypertension. There were 25 preterm births. Fourteen had early onset preterm and the rest eleven were late preterm. Among these preterm births, 3 were spontaneous and 22 were induced.

Mode of delivery was vaginal for 27 patients and forty two had caesarean delivery. Six women with IUGR alone and five women with coexisting preeclampsia were also terminated in view of abnormal Doppler. In our study, we were able to establish a statistical significant association with neonatal outcome like small for gestational age, low Apgar at birth and acidosis on arterial blood gas analysis and respiratory distress syndrome.

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Conclusion

- We were able to establish association between unilaterally increased Pulsatility Index done at 18 to 20 weeks and adverse maternal & perinatal outcome.
- The uterine artery Doppler (unilaterally increased uterine artery Pulsatility index) at 18-20 weeks was highly predictive for maternal and perinatal outcome.
- Further, higher prediction rates were achieved when uterine artery Doppler (unilaterally increased PI) was combined with placental position (placental laterality).

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